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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/826,082	04/15/2004	Timothy C. Wang	UMY-043	1338

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EXAMINER	
BELYAVSKYI, MICHAIL A	
ART UNIT	PAPER NUMBER
1644	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	12/26/2006	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/826,082	WANG ET AL.	
	Examiner	Art Unit	
	Michail A. Belyavskyi	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-36* is/are pending in the application.

4a) Of the above claim(s) *5-12,23-27,34 and 35* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,13-22,28-33 and 36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment, filed 10/31/06 is acknowledged.

Claims 1-36 are pending.

2. Applicant's election with traverse of Group I, claims 1-4,13-22,28-33 and 36 in the reply filed on 10/31/06 is acknowledged. Applicant traverse the Restriction Requirement on the grounds that the search of Groups I and VI together would not constitute a serious search burden on the examiner and that search of the claims of Group I would provide useful information for the claims of VI.

This is not found persuasive because the MPEP 803 (August 2001) states that "For purposes of the initial requirement, a serious burden on the examiner may be prima facie shown if the examiner shows by appropriate explanation either separate classification, separate status in the art, or a different field of search". The Restriction Requirement enunciated in the previous Office Action meets this criteria and therefore establishes that serious burden is placed on the examiner by the examination of more than one Group. The Inventions are distinct for reasons elaborated in paragraphs 3-5 of the previous Office Action and above

The requirement is still deemed proper and is therefore made FINAL.

Claims 5-12, 23-27 and 34-35 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to nonelected inventions.

Claims 1-4,13-22,28-33 and 36 read on a method of determining whether a subject has an bone marrow derived stem cell dependent metaplasia, comprising detecting the presence of BMDC polypeptide are under consideration in the instant application.

3. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention *to which the claims are directed.*

4. Applicant's submission of International Search Reports on the IDS, filed 06/31/06 has been considered, however said citation has been crossed out as it is not appropriate for printing in an issued patent.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112.
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 16 –20 and 22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7. Dependent claim 16 recites "the level of BMDC or BMDC-derived cells". There is insufficient antecedent basis for this limitation in the claims, since base Claim 1 does not recite levels of BMDC or BMDC-derived cells.

8. Claim 22 is indefinite and ambiguous in the recitation of Flk-1,Sca-1 etc polypeptide in the second line. Recitation of a polypeptide without providing SEQ ID NO for the polypeptide is indefinite and ambiguous because different laboratories may have the same name for a different polypeptide.

9. Claims 1-4, 13-22, 28-33 and 36 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification disclosure does not enable one skilled in the art to practice the invention without an undue amount of experimentation.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the limited working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention.

The specification only discloses that : (i) BMDC are involved in healing of acute gastric ulvers (see Example 1 in particular) , (ii) inflammation and tissue loss secondary to chronic gastric *Helicobacter* infection represent a sufficient stimulus for long-term engraftment and homing of BMDC that might contribute over time to metaplasia, dysplasia and cancer(see Example 2 and 3 in particular). It is noted however, that specification disclosed that "**in our system we believed** that MSC is the most likely cell type responsible for engraftment seen (emphases added, see page 61 in particular). The Specification farther disclosed that it is suggested that the quality as well as the quantity and duration of inflammation plays a central role in the degree of maladaptive differentiation of the BMDC once it resides in the peripheral tissue . **The concept that cancer can arise from BMDC** would alter greatly our understanding of cancer intitiation and progression (emphases added). In other words, the Specification only prophetically suggested that MBDC might contribute to cancer.

The specification does not adequately conformed or show the existence of direct correlation between the presence of BMDC or BMDC –derived cells and probability that the subject has BMDC-associated cancer or BMDC dependent metaplasia. The Specification provide no evidences that the presence of BMDC or BMDC-derived cells in a test sample from the subject is an indicative that the subject has BMDC-associated cancer or BMDC dependent metaplasia or has a higher than normal risk of developing either an BMDC-dependent metaplasia or BMDC-associated cancer. Moreover, no animals models were used to study the effectively of a method of determining whether a subject has an BMDC dependent metaplasia or a method of determining whether a subject has BMDC-associated cancer or a subject has a higher than normal risk of development an BMDC dependent metaplasia or BMDC-associated cancer, each comprising detecting the presence of BMDC or BMDC-derived cells in the test sample from the subject . Since there is no animal model studies and data in the specification to show the effectively of a method of determining whether a subject has an BMDC dependent metaplasia or a method of determining whether a subject has BMDC-associated cancer or a subject has a higher than normal risk of development either an BMDC dependent metaplasia or BMDC-associated cancer, each comprising detecting the presence of BMDC or BMDC-derived cells in the test sample from the subject it is unpredictable how to correlate disclosed data with the claimed intended use. Lyden et al., (Nature Medicine, 2001, Vol.7, page 1194-1201) teach that it is not yet established whether BM-derived precursor cells can contribute to tumor neo-angiogenesis (see entire document, Abstract in particular). Feldman et al (Transplant. Proc. 1998, 30, 4126-4127) teach that "while it is not difficult to study the pathogenesis of animal models of disease, there are multiple constraints on analyses of the pathogenesis of human disease, leading to interesting dilemmas such as how much can we rely on and extrapolate from animal models in disease". Mestas et al (J. of Immunology, 2004, 172, pages 2731-238) teach that there exist significant differences between mice and humans in immune system development, activating and response to challenge in both the innate and adaptive arms. As therapies for human diseases become ever more sophisticated and specifically targeted it becomes increasing important to understand the potential limitations of extrapolating data from mice to humans. The literature is littered with the examples of therapies that work well in mice but fail to provide similar efficacy in humans.

Thus , one skill in the art can not predict the efficiency of: (i) a method of determining whether a subject has an BMDC dependent metaplasia, claimed in claim 1, or a method of determining whether a subject has BMDC-associated cancer, claimed in claim 2 or a subject has a higher than normal risk of development an BMDC dependent metaplasia, claimed in claim 3 or BMDC-associated cancer, claimed in claim 4, each comprising detecting the presence of BMDC or BMDC-derived cells in the test sample from the subject . In addition, Applicant himself acknowledge that is has been unexpected discovery that the loss of cells in inflamed tissue during chronic inflammation leads to the influx and long-term re-population of the tissue with bone marrow derived stem cells. As such, the invention must be considered unpredictable. Thus in the absence of working examples or detailed guidance in the specification, the intended uses of a method of determining whether a subject has an BMDC dependent metaplasia or a method of determining whether a subject has BMDC-associated cancer or a subject has a higher than normal risk of development an BMDC dependent metaplasia or BMDC-associated cancer, each comprising detecting the presence of BMDC or BMDC-derived cells in the test sample from the subject are fraught with uncertainties.

Thus, Applicant has not provided sufficient guidance to enable one skill in the art to use claimed (i) a method of determining whether a subject has an BMDC dependent metaplasia, claimed in claim 1, or a method of determining whether a subject has BMDC-associated cancer, claimed in claim 2 or a subject has a higher than normal risk of development an BMDC dependent metaplasia, claimed in claim 3 or BMDC-associated cancer, claimed in claim 4, each comprising detecting the presence of BMDC or BMDC-derived cells in the test sample from the subject in manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement. *In re Fisher*, 166 USPQ 18(CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

In view of the quantity of experimentation necessary, the unpredictability of the art, the lack of sufficient guidance in the specification, the limited working examples, and the limited amount of direction provided given the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

10. No claim is allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michail Belyavskyi whose telephone number is 571/272-0840. The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571/272-0841.

The fax number for the organization where this application or proceeding is assigned is 571/273-8300

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MICHAIL BELYAVSKYI, PH.D.
PATENT EXAMINER
12/20/06